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[54] **PROCESS FOR DIAGNOSING HYPERCYANOGENESIS**

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[51] **Int. Cl.**[2] **A61K 29/00;** A61K 31/68; G01N 31/00; G01N 33/16

[58] **Field of Search** 424/9, 129, 201

[56] **References Cited**

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[57] **ABSTRACT**

Hypercyanogenesis is diagnosed by injecting a human patient parenterally with hydroxocobalamine to produce cyanocobalamine, collecting the urine of the patient, decomposing the cyanocobalamine eliminated with the urine by photolysis, and determining the quantity of the thus-liberated hydrocyanic acid. The cyanide level following injection will vary, always initially increasing. In a normal patient, the cyanide level will rapidly thereafter fall to that of hypocyanosis; but in a patient afflicted with persistent hypercyanogenesis, the cyanide level will fall only relatively slowly toward its initial value.

1 Claim, No Drawings

PROCESS FOR DIAGNOSING HYPERCYANOGENESIS

It has been established, by clinical observations, that certain illnesses, such as disseminated sclerosis and certain algias, were at least partially caused by hypercyanosis. It has already been proposed to use hydroxocobalamine for counteracting acute cyanide poisoning caused by hydrocyanic acid, and for the treatment of various other illnesses. However, it has never been proposed to use hydroxocobalamine for diagnosing chronic hypercyanogenesis which, as set forth above, may be at least the partial cause of certain illnesses.

In normal health, a human being eliminates cyanide ions in the urine at a rate of approximately 1 gamma every 24 hours. When the quantity eliminated exceeds this figure, the cyanide ion content of the blood is too high, but it is important to be able to diagnose whether hypercyanogenesis is the cause of such illness.

The object of the present invention is to provide a process for diagnosing hypercyanogenesis by provoking hypercyanogenesis, that is to say, by provoking an accelerated elimination of the cyanide ions present in excess of normal in the blood.

The present invention is based on the analysis of the action of hydroxocobalamine on hydrocyanic acid and cyanide compounds in general and of clinical observations which have confirmed the possibility of using hydroxocobalamine as a diagnostic agent for hypercyanogenesis, this diagnostic agent simultaneously also having a curative action.

When hydroxocobalamine is in the presence of hydrocyanic acid or an aqueous solution of cyanide, one molecule of hydroxocobalamine combines with one molecule of hydrocyanic acid or cyanide with the formation of one molecule of cyanocobalamine. Since cyanocobalamine is not toxic, it has been proposed to use hydroxocobalamine, itself being almost completely harmless, to counteract acute cyanide poisoning.

On the other hand, it has become apparent that cyanocobalamine was much more mobile than hydroxocobalamine and that it was, at least partially, rapidly eliminated in the urine.

The present invention therefore provides a process for diagnosing hypercyanogenesis characterized in that a patient is injected parenterally with a high dose of hydroxocobalamine, the urine is collected, the cyanocobalamine expelled with the urine is decomposed by photolysis, and the thus-liberated hydrocyanic acid is quantitatively determined.

When the process was carried out, it was seen that, in the absence of any cause capable of producing a cyanuria of exogenous origin, the administration of hydroxocobalamine is followed by urinary hypercyanosis and this hypercyanuria may vary with the condition of the subject and is characteristic of a hypercyanogenesis appearing simultaneously with algias.

The dosage units of the present invention are preferably contained in injectable ampoules each containing a dose of 15 mg. of hydroxocobalamine.

The following clinical observations are given by way of examples for carrying out the process of the invention.

OBSERVATION NO. 1

On the first subject, the quantitative analysis was effected of the ions CN^- in gammas in the urine per 24 hours. The result of the analysis was 1γ. 24 hours after administration by intramuscular means of 5,000γ of hydroxocobalamine, this figure increased to 1.3γ. At the end of 48 hours, it had dropped back to 0.95 and a further injection was effected of 5,000γ of hydroxocobalamine, which caused the rate to climb back, 72 hours after the first injection, to 1.1γ. After 96 hours, i.e., 48 hours after the second injection, the rate had dropped back to 0.8γ.

It will be seen that this observation concerns a normal subject in which the injection of hydroxocobalamine temporarily increases the elimination of cyanide ions, but reduces the cyanide ion content of the blood below normal, which is translated into a hypocyanuria during the following periods.

OBSERVATION NO. 2

On a patient afflicted with disseminated sclerosis there was effected, before any treatment, the quantitative analysis of the CN^- ions in the urine, which showed 2.7γ per 24 hours. Then 5,000γ of hydroxocobalamine was administered by intramuscular means. The quantitative analysis of the CN^- ions in gammas per 24 hours was, 24 hours after injection, 8.9, 48 hours after injection, 0.7, and 72 hours after the said injection 0.9.

The subject was therefore afflicted with endogenous hydrocyanic auto-intoxication, the normal level of the urinary hydrocyanic acid being reestablished by a single injection of hydroxocobalamine.

OBSERVATION NO. 3

In a subject it was discovered, before any treatment, that 1.75γ of CN^- ions per 24 hours was present in the urine. The subject was subjected to several successive injections of hydroxocobalamine, namely, an initial injection of 10,000γ followed 24 hours later with an injection of 20,000γ, then an injection of 30,000γ 24 hours later, then an injection of 20,000γ every 24 hours.

The results of the analyses were as follows:

Time	Injection	CN^- in γ per 24 hours
0	10,000 γ	1.75
24h	20,000 γ	15.6
48h	30,000 γ	2.3
72h	20,000 γ	20.6
96h	20,000 γ	8.4
120h		3.0

It will be seen that the subject is afflicted with a persistent hypercyanogenesis, the administration of a new dose of hydroxocobalamine or a stronger dose causing a hypercyanuria which is even higher, without return to the normal cyanuria.

It will be seen that the diagnosis has made it possible to confirm on patients having, before any treatment, a hypercyanogenesis, the existence of a syndrome of an endogenous cyanide auto-intoxication. The biochemical sign represented by a high content of cyanide ions before any treatment is confirmed and is much more easily detectable since it is greater with the process according to the invention.

Prolonged observations on subjects afflicted with evolutive bouts of disseminated sclerosis have made it possible to confirm a very clear hypercyanuria, sometimes very high, since it may reach 80γ and more of uri-

nary hydrocyanic acid in the course of the evolutive bouts, the injection of the diagnostic agent simultaneously producing an absence or attenuation of the pain which had not been noticed during previous bouts.

From a consideration of the foregoing disclosure, therefore, it will be evident that the initially recited object of the present invention has been achieved.

Although the present invention has been described and illustrated in connection with preferred embodiments, it is to be understood that modifications and variations may be resorted to without departing from the spirit of the invention, as those skilled in this art will readily understand. Such modifications and variations are considered to be within the purview and scope of the present invention as defined by the appended claims.

Having described my invention, I claim:

1. A process for diagnosing hypercyanogenesis, comprising the steps of injecting a human patient parenterally with hydroxocobalamine, collecting the urine of the patient, decomposing the cyanocobalamine eliminated with the urine by photolysis, determining the quantity of the thus-liberated hydrocyanic acid, repeating said injecting and collecting and decomposing and determining steps at a plurality of predetermined equal intervals of time after the first said injecting step in respect of the same human patient, also performing said collecting, decomposing and determining steps prior to any said injecting step in respect of the same human patient, and comparing the thus-determined quantities of hydrocyanic acid with the quantities of hydrocyanic acid characteristic of a normal human patient at the same said intervals of time, thereby to detect the presence of hypercyanogenesis.

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